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Phytochemical Composition, Traditional Uses, and Health Benefits of Gymnema Sylvestre (Gudmar) Leaves Powder: A Review

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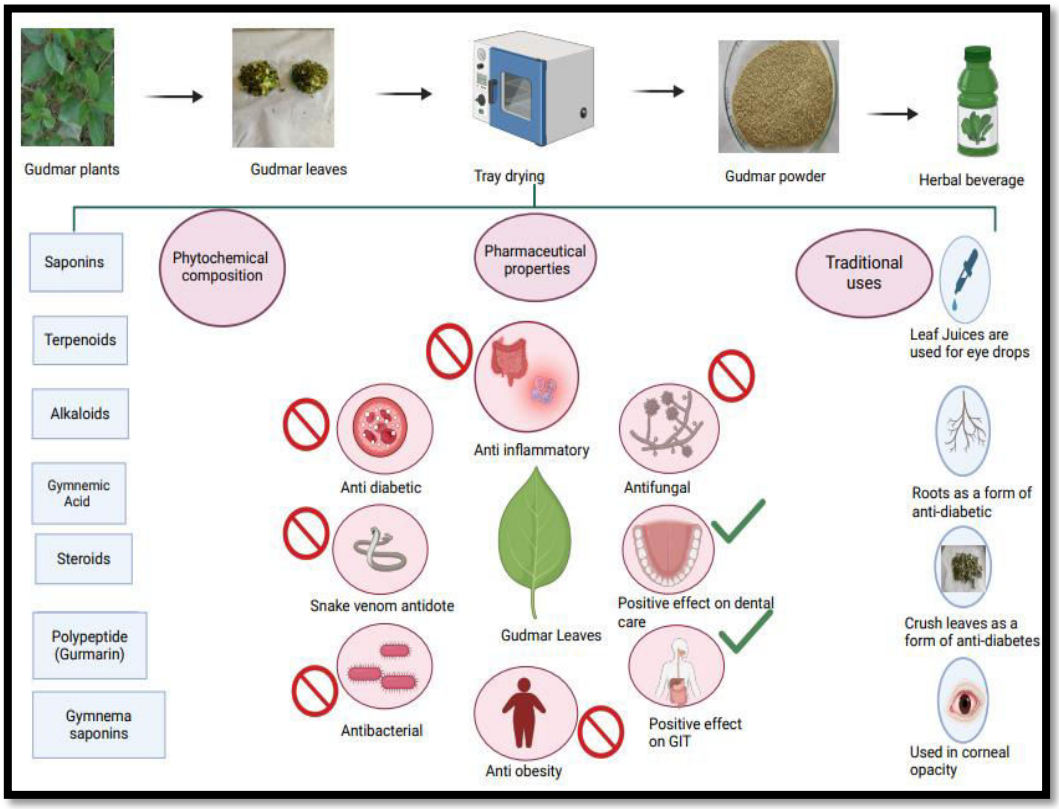
Abstract: Gymnema sylvestre, commonly known as Gudmar and belonging to the Asclepiadaceae family, has a rich history in Ayurvedic medicine. It is traditionally used to address various health issues such as kapha, pitta imbalances, ulcers, eye conditions, diabetes, and phlegm-related disorders when combined with flowers and bark. The herb is utilized in different dosing forms for managing diabetes and weight loss. Its phytochemical composition includes compounds like stigmasterol, triterpenoid saponins, Gymnemic acids, and gymnema saponins. Gymnemic acid, a key component, demonstrates anti-diabetic properties through diverse mechanisms. It showcases a range of functional and pharmacological properties, including anti-diabetic, anti-microbial, anti-inflammatory, dental care, anti-fungal, and anti-obesity activities. It also shows potential in addressing the link between obesity, diabetes, and Gymnemic acid, along with benefits for the gastrointestinal tract and as a snake venom antidote. The herb holds promise for future applications and research in various health-related areas.

Keywords: -Gymnema sylvestre, Phytochemical composition, Anti-diabetic properties, Therapeutic applications, Gymnemic acid, Pharmacological properties

Graphical Abstract



1 Introduction

Gymnema sylvestre commonly known as Gudmar belong to the Asclepiadaceae family, order Gentianales, a perennial, large woody climber, it is well-known in traditional medicine for its medicinal properties,which is found in much of the Indian subcontinent, Africa, and Australia, it is also widely distributed in India, particularly in the Banda region, the Konkan region, the Western Ghats region, the Deccan peninsula, and the western and northern parts of India[1]. In India, it can be found in the forests of Tamil Nadu, Uttar Pradesh, West Bengal, Kerala, Madhya Pradesh, Andhra Pradesh, Bihar, and Chhattisgarh. The plant is becoming rare and is being extensively cultivated in southern Indian states, especially Tamil Nadu, as a result of the plant's high demand in Asia.[2]. The fresh leaves which are mainly the economic part of the plant were green in colour and elliptical in shape, with an average weight of 0.157 grammes, length of 4.46 cm, and width of 2.56 cm. The flower is small and yellow, and it grows in clusters. The part that holds the seeds in is long and skinny, and it can be up to 3 inches long. The base of the leaf is rounded or heart-shaped, with 6–13 mm long pubescent petioles; the leaf is ovate-elliptic, acute, or shortly acuminate, and pubescent on both sides. Fruits ripen from March to May, while flowers bloom from October to January[3].The powdered substance has a mildly greenish yellow hue, a bitter flavour, and a pleasant, fragrant aroma[4].

Research on the plant through experimentation has begun at the very beginning of the 1930s with the publication of the first report on the plant's pharmacological

activity [5]. Dried leaf powder is used in the formulation of various products and medication compositions[6]. Gymnemic acid, a bioactive compound, is a naturally occurring component of plant leaves that can help lower blood sugar levels in different ways. It helps our bodies make more insulin, which controls blood sugar. It also helps our bodies release more insulin, stops our bodies from absorbing too much sugar from food, and helps our bodies use sugar better by increasing the activity of certain enzymes [7]. It is also used in the form of a simple tea brew, tea bags, beverages, and confectioneries or in health supplements[8,9].Itis the second bestselling medicinal plant in the world market requiring a cost-effective and simple method of cultivation to meet its growing demand [3].

2 Traditional Uses in Ayurvedic Medicine

Since prehistoric times, people have utilised plants and products derived from them for medical purposes. Plant sources are investigated and found to provide the new chemical entities needed for medical purposes. India's cultural history includes the development of Ayurveda and plant-based therapies for health care through everyday life experiences[10]. The primary source of healthcare for approximately 80% of people in developing nations is traditional medicine, according to estimates from the World Health Organisation (WHO). The Indian subcontinent has contributed natural remedies like Ayurveda, Yunani, and Siddha to the medical world[11]. Itsleaves have great ayurvedic therapeutic potential; they are said to treat kapha, pitta, ulcers and eyes, diabetic therapy, and phlegm-related disorders when combined with the flowers and bark. Castor oil-triturated leaves offer substantial defence against enlarged glands and visceral organs like the liver and spleen[12]. Insect bites can be effectively treated by applying root paste externally, and piles can be effectively treated with root bark[13]. The Sahariya tribe of Madhya Pradesh, India, uses G. sylvestre to treat Parkinsonism, asthma, and corneal opacity in both humans and animals[14]. The leaves are used by the Kol tribe of Chhattisgarh, Rajasthan, the Godavari district (Andhra Pradesh), Kandla (Maharashtra), and the Nayaks of Karnataka to treat eye issues, diabetes, glycosuria, gastrointestinal issues, and urinary symptoms[15]. In many parts of India, GS has been used as traditional medicine. The Ayurvedic Pharmacopoeia of India states that among other conditions, svasa (bronchial asthma), kasa (cough), kustha (leprosy and other skin diseases), and vrana (wounds) can all be treated with gymnema, depending on the dosage form and formulation[16]. As an alexipharmic, anodyne, anthelmintic, bitter, astringent, cardiotonic, digestive, diuretic, laxative, stimulant, stomachic, and uterine tonic, G. sylvestre is used to treat a variety of conditions, including amenorrhea, asthma, bronchitis, conjunctivitis, constipation, cough dyspepsia, haemorrhoids, hepato-plenomegaly, intermittent fever, jaundice, and leukoderma. These descriptions are based on writings from various Indian medical systems[13]. The commercial products made from

Gymnema that are currently on the market include GlucoCare (Natural Blood Glucose Health), Diabecon (GlucoCare), Dia-Botica Capsules, Lean Care (weight management), Ayur Slim, herbal tea, and Meshashringi[17].

2.1 Dosing Forms

In Adult (age ≥18)

•Type 1 diabetes, GS powder (200 mg) has been taken twice day orally while careful insulin administration is maintained. Insulin dosages or those of other concurrent hypoglycemic medications may need to be changed or stopped while under a doctor's supervision. [18].

•Type 2 diabetes: 2 ml of an aqueous decoction (10 g of powdered leaves that have been shade-dried per 100 ml) has been taken three times a day, or 200 mg of GS4 has been taken orally twice a day. Insulin dosages or those of other concurrent hypoglycemic medications may need to be changed or stopped while under a doctor's supervision. For six months, six to fifteen drops of Gymnema sylvestre "Q" were taken twice or four times a day with 1/4 cup of water[18].

•Weight loss: extract (GSE; 400 mg) has been investigated in conjunction with niacin-bound chromium (NBC; 4 mg) and a water-soluble, calcium-potassium salt of (−)-hydroxycitric acid (HCA-SX) (4,667 mg)[19].

An overview of Gymnema sylvestre and its claims in different regions of India is provided in the following Table 1 [20].

Table No. 1Folklore medicine claim in various part of India.

Sr. No.	Name of the State	Folklore Claim	References
1.	Andhra Pradesh	Leaf juice is used as eye drops in the Medak district of Andhra Pradesh; leaf powder is prescribed for diabetes and stomach problems.	[21]
2.	Chhattisgarh	Entire plant for its anti-inflammatory and anti-asthmatic properties, and its leaves for their diuretic properties. This plant is used in Jashpur District to treat dysentery, ulcers, and vomiting.	[22] [23]
3.	Karnataka	Its roots are used in the Karnataka district of Gulbarga as an anti-diabetic.	[24]
4.	Kerala	In Kerala, Gymnema sylvestre leaves are crushed with water and their juice consumed prior to meals as a treatment for diabetes.	[25]
5.	Tamil Nadu	To treat animals with ephemeral fever, Gymnema sylvestre leaves are ground along with pepper, garlic, and a small amount of common salt.	[26]

		Leaf juice is applied to corneal opacity.	
6.	Uttar Pradesh	Patients with cataracts in the Jhansi district of Uttar Pradesh are administered fresh leaf paste twice a day.	[27]
7.	Pondicherry	Water is given along with 2-3g of powdered dried leaf. For 15 days, a daily dose of seven fresh leaves in the morning is prescribed for diabetes.	[28]

3 Phytochemical Composition

Numerous phytochemicals with anti-inflammatory properties found in gymnema species include saponins, terpenoids, flavonoids, tannins, steroids, and alkaloids[29,30]. Saponins possess antifungal, antidiabetic, and hypocholesterolemic qualities[31]. in contrast, terpenoids help lower blood sugar levels, activities of the central nervous system are caused by steroids and saponins[32]. Phytochemical screening of leaf extracts indicated the presence of cardiac glycosides, alkaloids, flavonoids, steroids, and saponins[33]. It possesses several medicinal qualities, including antibacterial, antioxidant, antipyretic, and antidiabetic agents, which can be attributed to its phytochemical content[34]. Flavonoids can fight infections and have antiallergic, antimicrobial, anti-inflammatory, and anticancer properties[35].

Table 2- Phytochemical compounds of Gymnema sylvestre

Sr.No.	**Phytochemical compounds**	**Mode of Action**	**eferences**
1	Saponins	Antifungal, Antidiabetic, and Hypocholesterolemic qualities.	[31]
2	Terpenoids	Help lower blood sugar levels	[36]
3	Alkaloid	Hypoglycaemic activity	[1]
4	Gymnemic acid A1 and its derivatives.	Anti-sweet activity.	[37]
5	Steroids and saponins	Activities of the central nervous system	[36]
6	Flavonoids	Fight infections and have antiallergic, antimicrobial, anti-inflammatory, and anticancer properties	[35]
7	Triterpenoid saponins	Possess anti-tumor, anti-fungal, hepatoprotective, and anti-diabetic effects in numerous studies.	[38]
8	Gymnemasaponins (Gymnemagenin and	Hypoglycemia in motion. B cell proliferation. Gymnemagenin	[39]

	Gymnestrogenin)	prevents the absorption of glucose.	
9	Polypeptide (Gudmarin)	Reduce the number of sweet carvings by blocking the perception of bitter or sweet flavours.	[1]

Gymnema sylvestre stems were found to contain a variety of chemical components that are therapeutically significant, including stigmasterol and triterpenoid saponin find out by withchromatographic techniques. Numerous health benefits are provided by stigmasterol molecules, such as hypoglycemia, anti-diabetic, antioxidant, and anticancer effects. Triterpenoid saponins have been found to possess anti-tumor, anti-fungal, hepatoprotective, and anti-diabetic effects in numerous studies [38]. Gymnemic acids and gymnema saponins, which are categorised as oleanane saponins, are the main chemical components of this plant. The oleanane and dammarane types of saponins are present in Gymnema sylvestre leaves [40].In addition to saponins, this plant's leaves contain cardiac glycosides, anthraquinones, and other substances[41]. Moreover, this plant contained phenols, quinones, flavonoids, and tannins[42].The leaves also contain the anthraquinone derivatives, organic acid (5.5%), parabin, inositole alkaloids, calcium oxalate (7.3%), lignin (4.8%), cellulose (22%) and resins, chlorophyll, albumin, tartaric acid, formic acid, carbohydrates, butyric acid, and alkaloids[43].The 3-O-glucouronide of gymnemagenin (hexahydroxy-olean-12-ene) is found in gymnemic acids, along with several acylated (tiglolyl, methylbutyroyl, etc.) derivatives of it. The individual gymnemic acids (saponins) are gymnemic acids I–VII, gymnemosides A–F, and gymnemasaponins. It has been demonstrated that G. sylvestre contains a variety of compounds, including stigma sterol, (+) quercitol, lupeol, (-) amyrin, and gymnemic acids. Kaempferol 3-O-beta-D-glucopyranosyl-(1,4) is a newly identified flavonol glycoside. -(1,6) alpha-Lrhamnopyranosyl. It has also been reported that G. sylvestre aerial portions contain -beta-D-galactopyranoside [4]. It has been found that there are three new oleanane type triterpene glycosides like beta-O-benzoylsitakisogenin 3-O-beta-D-glucopyranosyl (1,3), Longiospinogenin 3-O-beta-D-glucopyranosyl (1,3) potassium salts-beta-D-glucopyranoside and 3-O-beta-D-glucopyranosyl (1,3) in 29-hydroxylongispinogenin-beta-D-glucopyranoside and the alternoside II sodium salt were extracted from an ethanolic Gudmar extract. In addition, gymnestrogenin, a novel pentahydroxytriterpene that was extracted from leaves, has been reported[43]. Other plant compounds include lupeol, -amyrin related glycosides, tartaric acid, formic acid, butyric acid, hentriacontane, pentatriacontane, phytin resins, dquercitol, and chlorophylls. Alkaloids in the plant extract also tested positive[44].

4. Mechanism of action of Gymnemic Acid

It has been shown to have anti-diabetic properties through a number of different mechanisms. It can lower blood sugar levels by blocking the intestines' ability to

absorb sugar molecules[9]. The medication acts by stimulating the pancreatic secretion of insulin[45]. The following are some potential mechanisms through which the leaf extract, also known as gymnemic acid, exerts its hypoglycemic acid effects involves 1. It stimulates islet cell regeneration; 2. It raises insulin secretion; 3. It inhibits intestinal glucose absorption; 4. It increases glucose utilisation by activating the enzymes that use [36].Glucose through insulin-dependent pathways, such as phosphorylase; reducing sorbitol dehydrogenase; and increasing phosphorylase activity[11]. Affinity Ultrafiltrationhave quick screening reveals the presence of α-glucosidase inhibitors[46]. It has been reported to decrease the activity of insulin-independent enzymes such as glycogen phosphorylase, gluconeogenic enzymes, glucose 6-phosphatase, fructose 1,6-diphosphatase, and sorbitoldehydrogenase, which also increases phosphorylase activity, and to increase the activity of insulin-dependent enzymes such as hexokinase, glycogen synthetase, glyceraldehydes 3-phosphate dehydrogenase, and glucose 6-phosphate dehydrogenase [38].Gudmar in functions similarly by interfering with the tongue's taste buds' capacity to distinguish between sweet and bitter flavours. The hypoglycemic effect of gymnemic acids is a result of a series of actions that begin with the modulation of incretin activity, which in turn causes the release and secretion of insulin. Additionally, it promotes pancreatic islet cell regeneration for improved glucose uptake by enzymes[9]. This procedure interferes with the ability of mouth and intestinal receptors to sense sweetness and reduces the small intestine's absorption of glucose and fatty acids. The literature has previously reported that the mechanism of action of gymnemic acid is similar to that of incretin-mimetic[47]. Research has revealed that glyceraldehyde-3-phosphate dehydrogenase (GAPDH), an essential enzyme in the glycolysis pathway, interacts with gymnemic acid [48].The research also showed that gymnemic acid's acyl moieties are essential for GA-induced smearing of GAPDH and G3PDH as well as for GA derivatives' antihyperglycemic properties. [49]. According to a study, this plant's methanol extract had a greater impact on β-cell regeneration. This led researchers to hypothesise that the plant could treat type I diabetes by fully restoring pancreatic cell function[50].

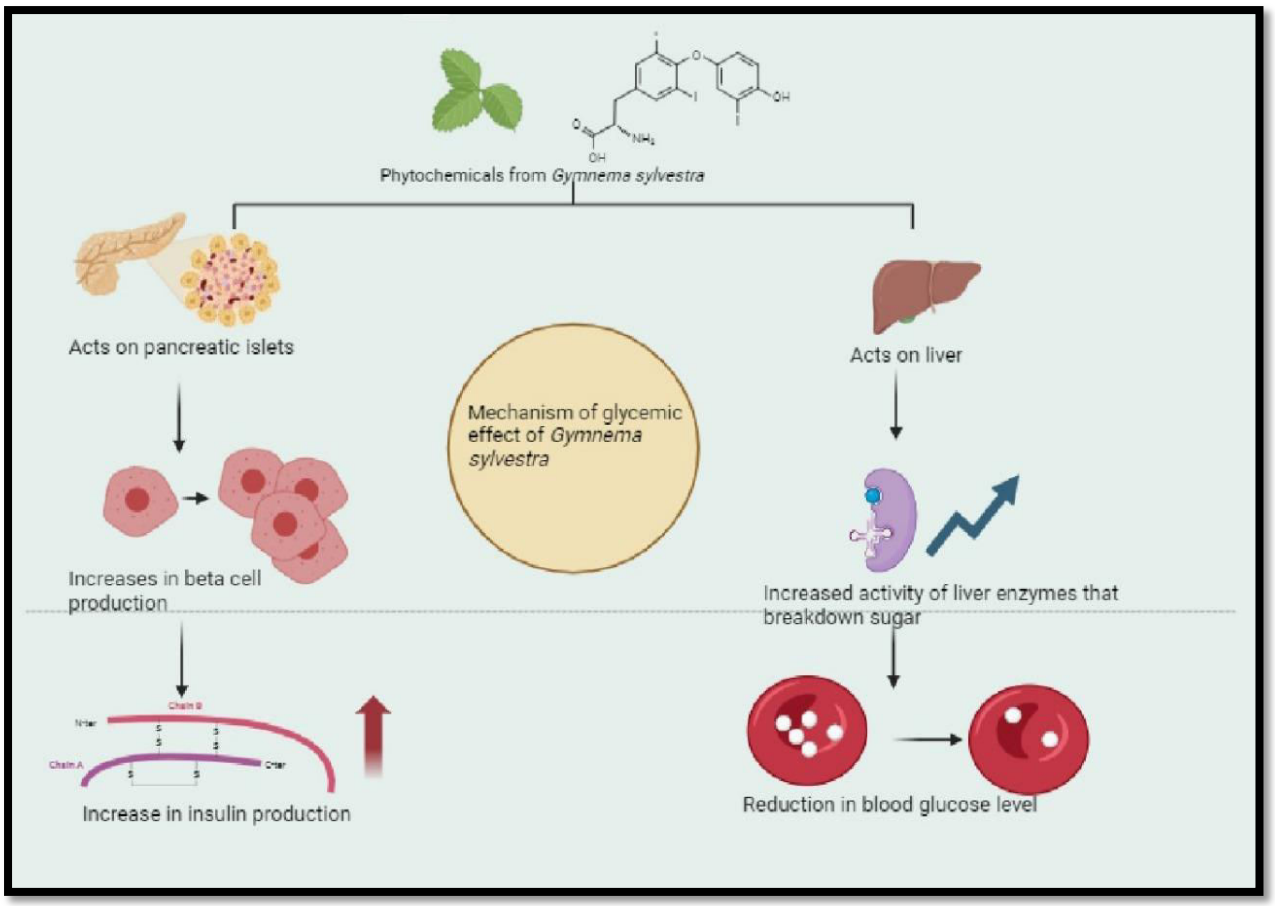


Fig 1: - Mechanism of gymnemic acid

5. Functional and Pharmacological properties ofGymnema sylvestre

It has a long history of usage in traditional medicine across the world[51]. It is also considered as a medicinal plant with the ability to treat various ailments (Fig. 1) and is widely recognised for its sweet flavour suppressing effect and is utilised in the treatment of anti-diabetes. It is also used to combat obesity as food additives.A group of authors earlier defined some medicinal plants and biological organisms (macrofungus) as a gold gift to human race. Some of the herb's important pharmacological qualities have been thoroughly discussed[9].

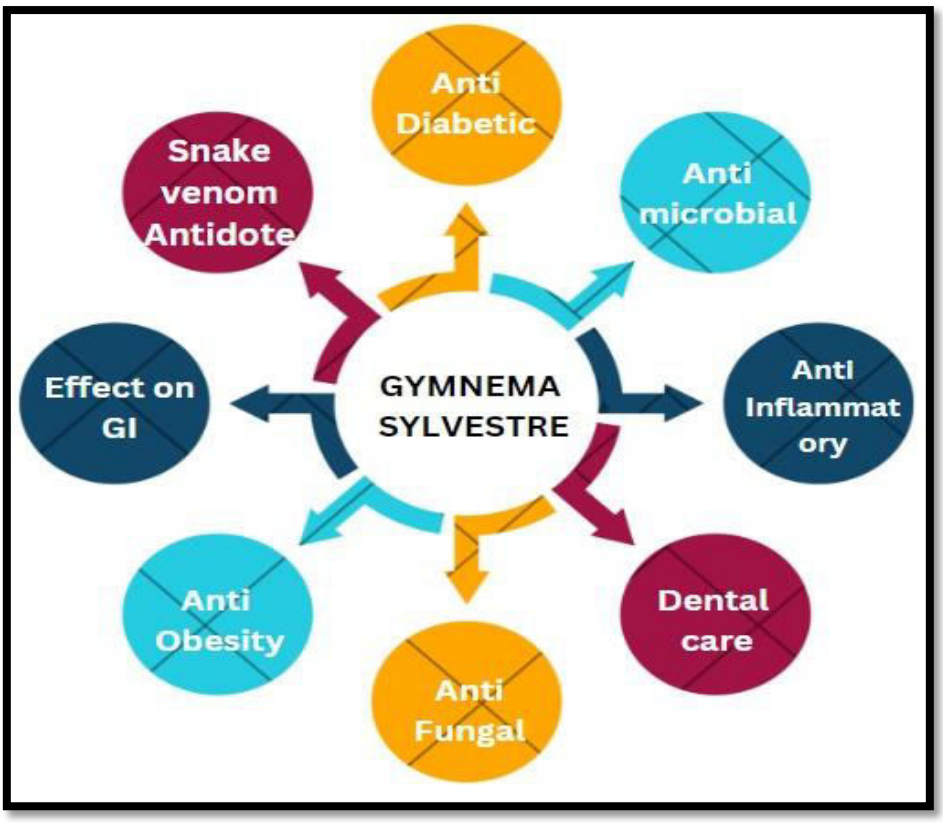


Fig 2: Pharmacological Properties of Gymnema sylvestre.

5.1 Anti-Diabetic Activity

G. sylvestre, a plant extract, decreases serum glucose levels and enhances glucose tolerance, which may be helpful in certain non-insulin-dependent diabetes cases[10]. It was first noted that the leaves had hypoglycemic properties in the late 1920s. Compared to many hypoglycemic medications, which have a quick effect, the plant's hypoglycemic activity is mild. Through the regeneration of pancreatic insulin-secreting cells, gymnema leaves raise insulin levels [43]. In patients with diabetes, lowers urine glucose levels and inhibits adrenohypophyseal activity as well as the adrenaline's hyperglycaemic response, which is thought to be controlled by phosphorylase and gluconeogenetic activity. There is ample evidence of the plant's hypoglycemic effects in normal diabetics.[13]. Sugiharastudied Gymnemic acid IV and discovered that it enhanced plasma insulin levels, which contributed to the antihyperglycemic effect of leaves. Om Santal Adivasi (OSA), a high molecular weight fraction isolated from leaf extract, stimulates insulin secretion from isolated human islets in a reversible manner, and its insulin secretagogue effects in MIN6 cells and human islets were partially dependent on the presence of extracellular Ca2+[49]. These findings suggest that modest concentrations of the G. sylvestre isolate OSA promote insulin secretion in vitro, at least in part due to Ca2+ influx, without impairing -cell survival [52,53]. In humans, OSA reduces

blood glucose levels while increasing plasma insulin and C-peptide levels. In vitro studies suggest that at least some of these effects can be attributed to a direct stimulatory effect on insulin secretion from -cells in the islets of Langerhans[54]. Following a study of the findings of various studies, it was shown that G. sylvestre leaves cause hypoglycemia in laboratory mice to treat the start of diabetes mellitus (NIDDM). When a diabetic patient is given Gymnema leaf extract, the pancreas is stimulated, resulting in increased insulin output. Paliwal evaluated if Gudmar leaf powder had favourable and promising effects on blood glucose levels in an animal investigation. There was no negative effect on the patients' health, therefore it can be stated that Gudmar powder is beneficial in decreasing fasting and postprandial blood glucose levels[8][55][56].

5.2 Anti-microbial activity

The leaf extracts have been shown to have moderate effectiveness against three pathogenic Salmonella species (Salmonella typhi, S. typhimurium, and S. paratyphi). The aqueous extract outperformed the other extracts in terms of effectiveness against Salmonella species [57]. Extracts of the aerial portions of in ethanol, chloroform, and ethyl acetate have also been found to exhibit antibacterial activities against P. vulgaris, E. coli, P. aeroginosa, Klebsellapneumoniae, and S. aureus. Human mucosal, disseminated, and invasive infections are caused by the fungus Candida albicans. The triterpenoid saponin family of gymnemic acid inhibits the growth of Candida albicans. Purified gymnemic acids decreased the conversion of yeast to hypha in a variety of hypha-inducing conditions, including the presence of serum, but did not effect on the growth or survival of cells[58]. Because it has larvicidal activity against Culex tritaeniorynchus, the vector of Japanese encephalitis, it can play a significant role in the vector control program [59]. The antimicrobial activity of aerial and root sections was evaluated independently, as demonstrated by Bhuvaneswari, the results shown the broad-spectrum action of methanol extracts in the acidic range against all infections[60]. Extracts of the fruit and roots of G. sylvestre showed zones of inhibition at a dose of 100 mg/ml. Many bacterial species, including Staphylococcusaureus (8.7 mm), Bacillussubtilis (11.66 mm), Escherichiacoli (13 mm), Klebsiellaaerogenes (12 mm), and Aspergillusniger (10.75 mm), are inhibited by G. Sylvestre fruit extract. Staphylococcusaureus (11.5 mm), Bacillussubtilis (10.66 mm), Escherichiacoli (15.5 mm), Klebsiellaaerogenes (mm), and fungal species like Aspergillusniger (11.33 mm) are all inhibited by G. Sylvestre root extract.

5.3 Anti-Inflammatory Activity

The leaf of G. sylvestre is considered bitter, acrid, thermogenic, digestive, liver tonic, anodyne, and anti-inflammatory in the Ayurvedic medical system. The anti-inflammatory properties of G. sylvestre are attributed to its bioactive components, specifically its tannins and saponins [9].The study used the cotton

pellet method and carrageenin-induced paw edoema to examine the anti-inflammatory effects of an aqueous extract of G. sylvestre leaves in rats at doses of 200, 300, and 500 mg/kg. Within 4 hours of administration, the fluid concentrate at 300, 26 mg/kg reduced the edoema volume by 48.5% in comparison to the control paw edoema volume, while the standard medication, phenylbutazone, decreased the edoema volume by 57.6%. Granuloma weight was significantly reduced by the watery concentrate at dosages of 200 mg/kg and 300 mg/kg in comparison to the control group [61].
Mice were subjected to an in vivo two-stage carcinogenesis model employing 12-O-tetradecanoyl phorbol-13-acetate (TPA) as a promoter and 7,12-dimethylbenz[a]anthracene as an initiator[62].

5.4 Dental Cares Treatment

The progress and development of dental caries are associated with the presence of multiple Gram-positive bacteria species. Dental plaque is produced by primary cariogenic bacteria, including S. mutans, S. aureus, S. mitis, and the fungus Candida albicans. The plaque adheres to tooth surfaces through the production of extracellular polysaccharides. After that, the bacteria transform glucose into organic acids, which cause dental enamel to become less mineral-rich. It follows that eliminating cariogenic bacteria from the oral cavity is essential. But remember that a lot of these have some resistance to antibiotics like ampicillin, clindamycin, and chloramphenicol [63]. An effective substitute for antibiotics, which are costly and can cause adverse effects like gastrointestinal issues, would be plant extracts, which have long been used for dental hygiene because of their strong antibacterial activity. Among them a study conducted by [63] examined the efficacy of multiple GS extracts in preventing dental cavities, with the methanol extract exhibiting the strongest antimicrobial activity [64].Tested against microbial dental infections at 25, 50, and 100 mg/mL, the chloroform, petroleum ether, and methanolic leaf extracts of G. sylvestre were found to be significantly effective against these cariogenic bacteria; of these, the methanolic extract exhibited the highest activity at the lowest concentration. These herbal remedies will pave the way for novel approaches to the treatment of dental caries once they have received scientific community clinical approval[64].

5.5 Anti-Fungal Activity

Strong antifungal activity was shown by the crude and pure saponin fractions from GS leaves, which were up to three times more effective than amphotericin B, a common medication. More suppression was observed in Aspergillus fumigatus than in Aspergillus flavus and Aspergillus niger[65]. It seems to show that the antibacterial activity of plant extracts is caused by saponins, since the minimum inhibitory concentration values range from 600 to 1,200 mg/L. In the future, saponins may be used as a medication to treat and prevent Gram-negative bacteria and fungi[63]. A qualitative assessment was made of the GS methanolic

extract's antifungal efficacy. 30 grammes of Sabourad's dextrose agar (SDA) were dissolved and autoclaved in 1000 millilitres of distilled water. A six-well plate was filled with 2.5 mL of this mixture per well, and the mixture was left to harden. After scraping the mycelium of the fungus Fusarium oxysporum (MTCC 3322) and suspending it in 10 millilitres of SDA broth, mother broth was prepared aseptically. On separate wells of solidified SDA, 100 litres of methanolic extract were added in various doses ranging from 3 to 5 mg/ml. This was followed by 100 litres of mother broth. Additionally, the methanol solvent control was inoculated. Gold chloride and silver nitrate were examples of positive controls. After that, the plates were incubated at 37 degrees Celsius for three days, and then they were read[66].

5.6 Anti-Obesity activity

The two greatest diseases of the twenty-first century are obesity and type 2 diabetes. It is characterised by an increase in the build-up of fat molecules, or triglycerides, in adipose tissue, which leads to insulin resistance. Another way to describe it would be as a human condition where the body stores more fat than is necessary and can cause illness[16]. Resistin is a 12.5 kDa cysteine-rich protein that is exclusively present in white adipose tissue. It is also referred to as adipocyte-secreted factor and FIZZ3. It has been suggested that resistin may be a mediator between type 2 diabetes and obesity, and that elevated plasma resistin levels in obese mouse models may be causative in the development of insulin resistance [67].According to this theory, it has been demonstrated that the anti-diabetic medication rosiglitazone reduces the expression of resistin in mice's white adipose tissue. This suggests that inhibiting resistin expression may be one of the underlying mechanisms behind the protective effects of thiazolidinediones in insulin-resistant state. The antiobesity activity of a standardised G. sylvestre extract, niacin-bound chromium, and hydroxycitric acid was assessed by assessing changes in body weight, BMI, appetite, lipid profiles, serum leptin, and excretion of fat metabolites in the urine. It was discovered that the use of extract, hydroxycitric acid, and niacin-bound chromium was a safe and efficient weight loss method that promoted healthy blood lipid levels and helped reduce excess body weight and BMI [68].

5.6.1 Investigating the link between Obesity, Diabetes and Gymnemic acid.

Although the molecular mechanisms underlying the association between diabetes and obesity have long been unclear, recent findings indicate that the two most prevalent metabolic disorders may be linked by an enzyme [11]. The main outcome of fat and carbohydrate accumulation is obesity. By preventing carbohydrates from attaching to intestinal receptors, gymnemic acids help the body avoid "empty calories" and obesity. Like glucose, the acids can aid in the prevention of diabetes. Currently, gymnemic acids are provided for the treatment of obesity in the form of gymnema tea[69].

5.6.1.1 Experimental studies

In Elluru, India, 60 moderately obese participants (ages 21-50, BMI >26 kg/m (2)) participated in an 8-week randomised, double-blind, placebo-controlled human trial. G. sylvestre extract, in conjunction with (-)-hydroxycitric acid and niacinbound chromium, acts as an effective and safe weight-loss solution, assisting in the reduction of excess body weight and BMI[68]. Gymnemic acids inhibit the binding of carbohydrates to receptors in the intestine, so eliminating "empty calories" and preventing the body from becoming obese. By a similar manner, gymnemic acids can also help to control diabetes[11]. Its extract was found to significantly lower body mass index, organ weights, and visceral fat pad weight in cellular obesity induced by high-fat diets. By lowering levels of leptin, insulin, dyslipidemia, apolipoproteins, lipids, visceral fat pad weights, and oxidative stress in obese rats fed a high-fat diet, G. sylvestre extract may have anti-obesity effects[70]. Because it lowers body weight, food consumption, visceral organ weight, and levels of triglycerides, total cholesterol, low-density lipoproteins, very low-density lipoproteins, atherogenic index, glucose, and high-density lipoproteins, the saponin-rich fraction of aqueous leaf extract has anti-obesity activity. The water-soluble fraction of extract (120 mg/kg, p.o. for 21 days) showed anti-obesity efficacy in rats fed a high-fat diet. It lowers levels of apolipoproteins A1 and B, glucose, insulin, leptin, blood sugar, body weight gain, food consumption, serum lipids, and lactate dehydrogenase while raising HDL and antioxidant enzyme levels. The research found that the extract of had an antiobesity effect [71].

Utilising a lot of gymnemic acid in your diet can help you control your weight. Research on the effects of GA in the diet of Otsuka Long-Evans Tokushima Fatty (OLETF) rats, an obese animal model of type II diabetes, shows that in fact, GA can impede the absorption of oleic acid [63]. The study found a reduction in body weight and the amount of feed and water consumed (by roughly 1/3 and 2/3, respectively). Upon completion of the study, there was a nearly one-third reduction in total cholesterol and an approximate half reduction in LDL + VLDL cholesterol. The level of blood serum triglycerides was lowered to 25% of the control level for OLETF[72]. Additionally, the outcomes demonstrated that GA inhibition was reversible and dose-dependent, with a recovery process and inhibition level comparable to that of glucose absorption. Thus, GA had no withdrawal rebound effects on body weight and helped with weight loss by lowering hyperlipidemia [21].

5.7 Effect on Gastrointestinal tract

Acid production was lowered by almost 50% when using gymnema sylvestre or pure crystalline components containing gymnemate potassium salts. water soluble extract suppressed spontaneous contraction and inhibited KCl-induced muscle contraction in rat intestinal circular muscles, which may account for the plant's ability to relax intestinal muscle through the participation of endothelial-

derived hyperpolarizing factor and nitric oxide [5]. Gymnema sylvestre methanolic extract demonstrated anti-ulcer activity in rats with ulcers caused by Indomethacin, a forced swim stress model, and pylorus-ligated Wister rats. It raised the pH of gastric juice and significantly reduced the ulcer index ($p<0.01$), free acidity, total acidity, and gastric volume. The anti-ulcer effect was suggested to be caused by the presence of phytochemical components such as triterpenoids, alkaloids, resins, sterols, glycosides, carbohydrates, and proteins[73]. It has been reported that a herbomineral formulation containing extract improves intestinal transit and poor gastric emptying associated with diabetes. In this study, it was found that a formulation containing Gymnema sylvestre greatly improved intestinal transit and gastric emptying time ($p<0.001$ and $p<0.001$, respectively). Nonetheless, it was discovered that significantly decreased the secretion of glucose-stimulated gastric inhibitory peptides in wiener rats ($p<0.05$). In An ethanolic leaf extract was found to mitigate ethanol-induced mucosal damage in Wister Albino rats. Rats treated with this plant extract showed significant decreases in total proteins ($p<0.01$), non-protein sulfhydryl groups ($p<0.001$), stomach-wall mucus ($p<0.001$), and nucleic acids (p 0.001)[38]. In a study where gastric ulcers were induced in male Swiss Albino mice, the plant's aqueous extract was found to have anti-ulcerative properties. Treatment with the extract demonstrated significant ($p<0.05$) protective activity against aspirin-induced ulcers in rat models[74].

5.8 Snake Venom Antidote

It was tested if K gymnemate, which was extracted from the plant, could inhibit the ATPases that were separated from the venoms of V. russelli and N. naja. ATPases from venom were extracted and characterised by means of a one-step chromatographic technique. Gymnemate bound to the same site(s) that a spectrofluorimetric technique examined, blocking these fractionated ATPases, which are toxic components of the venom[5].

6. Toxicology Reports

In toxicology studies, it has been shown that consuming the right amounts of extract is safe. High doses can cause hypoglycemia, muscular dystrophy, weakness, shakiness, and excessive perspiration as side effects. Over the course of the 52-week trial, no animals died and there were no negative effects from feeding Wistar rats 1.00% basal powder (GSE)[75].It's used in diabetic patients has been associated with drug-induced liver injury (DILI) or toxic hepatitis [76]. When taking gymnema on an empty stomach, mild gastrointestinal distress may occur. Extremely high doses have the potential to induce hypoglycemia in susceptible individuals [13].

7. Future Aspects

The traditional and ethnobotanical uses of natural chemicals, especially those derived from plants, have garnered a lot of attention recently due to their extensive efficacy testing and generally accepted safety for human consumption. The traditional Ayurvedic medical system derived its foundation from medicinal plants. Currently, herbal therapeutics are becoming more and more popular as molecular targets in drug development as well as pharmacological applications. Humanity is seriously threatened by the growing trend of rising disease incidence and associated problems with commercial pharmaceuticals. Gymnema leaves have long been utilised in natural medicine clinics; in India, they have been used for aeons to support normal blood sugar levels. The flavour of gymnema dulls the sense of sweetness. It holds a significant position among medicinal plants that fight diabetes. It raises insulin levels and has shown anti-diabetic efficacy in studies and clinical settings. Since every part of G. sylvestre has some medicinal properties that can be used to good use. Recent decades have seen significant advancements in biological activity and applications for medicinal value. Saponins, flavonol, glycosides, gymnemanol, Gudmar in, and other substances are present in it.phytochemicals have a variety of pharmacological properties, including those that are anti-inflammatory, anti-oxidative, anti-metastatic, anti-diabetic, and lipid-lowering. It can therefore be used to make industrial products that are used to treat diabetes mellitus. The plant's medicinal value has grown, especially in light of numerous researchers' reports of its anti-diabetic properties. Nevertheless, the exact mechanism of action remains unknown.

7. Conclusion

Among naturally occurring substances that alter sweetness, Gymnemasylvestre holds a special place. As a botanical companion, It exhibits potential in terms of health and wellbeing. The herb has been used for many medicinal purposes as a traditional ayurvedic medicine since ancient times, and its use has grown in popularity in the contemporary era. When taken as part of a balanced diet, contains 75% of gymnemic acid from the leaf extract, which supports the pancreas nutritionally and helps to keep blood sugar levels in check. Because G. sylvestre has medicinal properties in all forms, it is a highly commercially exploitable plant. Over the past few decades, significant progress has been made regarding its physiological function and potential medical applications. As a result, it might be regarded as a source for commercial goods meant to cure diabetes and other long-term illnesses.

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